MEDICAL MUTUAL®

Drug Policy

Policy:	**202001-MRx (10-23)**	**Initial Effective Date: 01/16/2020**
Code(s):	**HCPCS J0896**	**Annual Review Date: 10/19/2023**
SUBJECT:	**Reblozyl ® (luspatercept-aamt)**	**Last Revised Date: 10/19/2023**

☐Subject to Site of Care

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

POLICY STATEMENT

This policy involves the use of Reblozyl. Prior authorization is recommended for medical benefit coverage of Reblozyl. Approval is recommended for those who meet the conditions of coverage in the **Initial Approval and Renewal Criteria, Preferred Drug (when applicable), Dosing/Administration, Length of Authorization, and Site of Care (when applicable)** for the diagnosis provided. The requirement that the patient meet the Criteria and Preferred Drug for coverage of the requested medication applies to the initial authorization only. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy.

The site of care medical necessity criteria applies to initial therapy and reauthorizations under the medical benefit only.

I. Length of Authorization [1]

- Beta Thalassemia: Coverage will be provided initially for 15 weeks (5 initial doses) and may be renewed annually thereafter.
- Anemia Due to Myelodysplastic Syndromes: Coverage will be provided initially for 21 weeks (7 initial doses) and may be renewed every 6 months thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Reblozyl 25 mg single-dose vial: 2 vials every 21 days
- Reblozyl 75 mg single-dose vial: 2 vials every 21 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- Beta Thalassemia: 600 billable units every 21 days
- Myelodysplastic Syndromes: 800 billable units every 21 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age, unless otherwise specified**; **AND**

Universal Criteria [1]

- Females of reproductive potential have a negative pregnancy test prior to start of therapy and will use an effective method of contraception during treatment and for at least 3 months after treatment; **AND**
- Patient has not had a deep vein thrombosis or a thrombotic stroke which required medical intervention within 6 months prior to therapy; **AND**
- Other causes of anemia (e.g., hemolysis, bleeding, recent major surgery, vitamin deficiency, etc.) have been ruled out; **AND**
- Reblozyl is not being used as a substitute for RBC transfusions in patients requiring immediate correction of anemia; **AND**
- Patient has a baseline Hemoglobin (Hb) < 11.5 g/dL (if Hb is 11.5 g/dL or higher, the dose must be delayed until the Hb is 11 g/dL or less) *(**Note:** If an RBC transfusion occurred prior to dosing, the pretransfusion Hgb must be considered for dosing purposes. Lab values are obtained within 7 days of the date of administration);* **AND**

Beta Thalassemia † Φ [1,4,8]

- Patient has a documented diagnosis of beta thalassemia (excludes alpha-thalassemia and hemoglobin S/ß-thalassemia variants) as outlined by the following:
  - Patient diagnosis is confirmed by *HBB* sequence gene analysis showing biallelic pathogenic variants; **OR**
  - Patient has severe microcytic hypochromic anemia, anisopoikilocytosis with nucleated red blood cells on peripheral blood smear, and hemoglobin analysis that reveals decreased amounts or complete absence of hemoglobin A and increased amounts of hemoglobin F; **AND**
- Patient is red blood cell (RBC) transfusion dependent as defined by requiring 6-20 RBC units per 24 weeks; **AND**
- Patient does not have major end organ damage**§**, defined as any of the following:
  - Liver disease with an ALT > 3x the ULN or history of evidence of cirrhosis; **OR**
  - Heart disease, heart failure NYHA classification 3 or higher, or significant arrhythmia requiring treatment, or recent myocardial infarction within 6 months of treatment; **OR**

- Lung disease, including pulmonary fibrosis or pulmonary hypertension which are clinically significant i.e., ≥ Grade 3; **OR**
- Creatinine clearance < 60 mL/min

§Requests for patients deemed to have any major end organ damage will be reviewed on a case-by-case basis.

***Requests for patients <18 years will be considered on a case by case basis for those with high transfusion burden and symptomatic iron overload, history of alloimmunization, or history of transfusion reactions*

Anemia Due to Myelodysplastic Syndromes (MDS) † ‡ Φ [1,5-7]

- Patient has lower risk disease (IPSS-R very low, low, or intermediate-risk); **AND**
- Patient has required 2 or more red blood cell units over an 8-week timeframe; **AND**
- Patient has a diagnosis of one of the following:
  - Myelodysplastic syndrome (MDS); **OR**
  - Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T); **AND**
- Used in one of the following treatment settings:
  - Patient has symptomatic anemia with blasts <5% in bone marrow; **AND**
    - Patient has not received prior treatment with an erythropoiesis stimulating agent (ESA) (i.e., ESA naïve); **AND**
    - Serum erythropoietin <500 mU/mL; **OR**
  - Patient has symptomatic anemia with ring sideroblasts ≥15% (or ring sideroblasts ≥5% with an SF3B1 mutation); **AND**
    - Serum erythropoietin >200 mU/mL; **OR**
    - Patient has had an inadequate response to prior treatment with an ESA (i.e. epoetin alpha ≥ 40,000 units/week for at least 8 doses or darbepoetin alpha ≥ 500 mcg every 3 weeks for at least 4 doses); **OR**
    - Patient has a documented contraindication or intolerance to the use of an erythropoiesis-stimulating agent

† FDA Approved Indications; ‡ Compendia Recommended Indication(s); **Φ** Orphan Drug

IV. Renewal Criteria [1,5-8]

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Patient will not receive doses < 21 days apart; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: thromboembolic events, severe hypertension, extramedullary hematopoietic masses in patients with beta thalassemia, etc.; **AND**

Beta Thalassemia

- Patient is experiencing disease response as evidenced by a decrease in the number of RBC transfusions; **OR**
- For new starts: Patient has not achieved a reduction in RBC transfusion burden after at least 2 consecutive, initial (1 mg/kg) doses (6 weeks) and requires a dose increase to 1.25 mg/kg; **OR**
- Patient experienced a response followed by a lack/loss of response and requires a dose increase to 1.25 mg/kg (from 1 mg/kg)

Anemia Due to Myelodysplastic Syndromes (MDS)

- Patient is experiencing disease response as evidenced by a decrease in the number of RBC transfusions; **OR**
- For new starts: Patient has not achieved a reduction in RBC transfusion burden after at least 2 consecutive, initial (1 mg/kg) doses (6 weeks) and requires a dose increase to 1.33 mg/kg; **OR**
- Patient has not achieved a reduction in RBC transfusion burden after at least 2 consecutive, 1.33 mg/kg doses (6 weeks) and requires a dose increase to 1.75 mg/kg; **OR**
- Patient experienced a response followed by a lack/loss of response and requires a dose increase by one dose level from the level in which response was lost (not to exceed a dose of 1.75 mg/kg)

***Note**: Discontinue Reblozyl if a patient does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose level or if unacceptable toxicity occurs at any time.

V. Dosage/Administration [1]

Indication	Dose
Beta Thalassemia	The recommended starting dose is 1 mg/kg once every 3 weeks by subcutaneous injection. – Dose increases for insufficient response: If a patient does not achieve a reduction in RBC transfusion burden after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose, increase the Reblozyl dose to 1.25 mg/kg. Do not increase the dose beyond the maximum dose of 1.25 mg/kg.
Anemia Due to Myelodysplastic Syndromes (MDS)	The recommended starting dose is 1 mg/kg once every 3 weeks by subcutaneous injection. – Dose increases for insufficient response: If a patient is not RBC transfusion free after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose, increase

	the Reblozyl dose to 1.33 mg/kg. If a patient is not RBC transfusion free after at least 2 consecutive doses (6 weeks) at the 1.33 mg/kg dose level, increase the Reblozyl dose to 1.75 mg/kg. Do not increase the dose more frequently than every 6 weeks (2 doses) or beyond the maximum dose of 1.75 mg/kg. *Note: If, upon a dose modification (i.e., dose reduction), a patient loses response (i.e. requires a transfusion) or Hgb concentration drops by 1 g/dL or more in 3 weeks in the absence of transfusion, increase the dose by one dose level. Wait a minimum of 6 weeks between dose increases.*
– If a planned administration of Reblozyl is delayed or missed, administer Reblozyl as soon as possible and continue dosing as prescribed, with at least 3 weeks between doses. – Assess and review hemoglobin (Hgb) results prior to each administration. If an RBC transfusion occurred prior to dosing, the pretransfusion Hgb must be considered for dosing purposes. – Dose decreases/interruptions: In the absence of transfusion, if Hgb increase is >2 g/dL within 3 weeks or if the pre-dose Hgb is ≥11.5 g/dL, reduce the dose or interrupt treatment until the Hgb is ≤11 g/dL. – Reblozyl should be reconstituted and administered by a healthcare professional.	

VI. Billing Code/Availability Information

HCPCS Code:

- J0896 – Injection, luspatercept-aamt, 0.25 mg: 1 billable unit = 0.25 mg

NDC:

- Reblozyl 25 mg single-dose vial: 59572-0711-xx
- Reblozyl 75 mg single-dose vial: 59572-0775-xx

VII. References

1. Reblozyl [package insert]. Summit, NJ; Celgene, Inc: August 2023. Accessed September 2023.
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3. Galanello R and Origa R. Beta-thalassemia. *Orphanet J Rare Dis.* 2010 May 21;5:11. Available at: https://ojrd.biomedcentral.com/articles/10.1186/1750-1172-5-11. Accessed November 2019.

4. Origa R. Beta-Thalassemia. 2000 Sep 28 [Updated 2021 Feb 4]. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1426/. Accessed March 2023.
5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) luspatercept-aamt. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2023.
6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myelodysplastic Syndromes. Version 1.2023. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2023.
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DOI: 10.1056/NEJMoa1908892.
8. Cappellini MD, Viprakasit V, Taher AT, et al. A Phase 3 Trial of Luspatercept in Patients With Transfusion-Dependent β-Thalassemia. N Engl J Med, 382 (13), 1219-1231; 2020 Mar 26. PMID: **32212518.** DOI: 10.1056/NEJMoa1910182.
9. Beaudoin FL, Richardson M, Synnott PG, et al. Betibeglogene Autotemcel for Beta Thalassemia: Effectiveness and Value; Final Evidence Report. Institute for Clinical and Economic Review, July 19, 2022. https://icer.org/wp-content/uploads/2021/11/ICER_Beta-Thalassemia_Final-Report_071922.pdf.
10. Della Porta M, Platzbecker U, Santini V, et al; The Commands Trial: A Phase 3 Study of the Efficacy and Safety of Luspatercept Versus Epoetin Alfa for the Treatment of Anemia Due to IPSS-R Very Low-, Low-, or Intermediate-Risk MDS in Erythropoiesis Stimulating Agent-Naive Patients Who Require RBC Transfusions. Blood 2020; 136 (Supplement 1): 1–2. doi: https://doi.org/10.1182/blood-2020-140284.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C93.10	Chronic myelomonocytic leukemia not having achieved remission
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts

D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.Z	Other myelodysplastic syndromes
D56.1	Beta thalassemia

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
15	KY, OH	CGS Administrators, LLC

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

Prior approval is required for HCPCS Codes J0896